Original Article

New methods to differentiate cardiac and non-cardiac disease cats from thoracic radiographs

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Abstract

The objective of this study was to distinguish between cats with cardiac disease and non-cardiac disease by using parameters obtained from thoracic radiographs. This study was performed in 49 cats with a mean age of 7.7±4.79 years. Weight, sex and breed of all cats were randomly chosen. Echocardiography was used as a gold standard to diagnose cardiac disease and separate the cats into two groups, cardiac disease (n=31) and non-cardiac disease (n=18). Five parameters were measured from the right lateral radiographs including 1) the cardiac length (L), 2) the cardiac width (W), 3) the width of the caudal vena cava (CVC), 4) the height of the spinous process of the fourth thoracic vertebrae (sT4), and 5) the length of the fourth sternal thoracic bone (S4). Ten formulae were designed from the five parameters. Five of these formulae produced an outcome showing a significant difference between the two groups ($p<0.05$). These formulae included L•W, L•W/sT4, L•W/S4, SUM_{LW}/S4, and SUM_{LW}•CVC. This study recommends the formulae L•W (cut-off >16.45 cm^2; sensitivity of 82.2% and specificity of 67%) and L•W/S4 (cut-off >12.85 cm; sensitivity of 81.7% and specificity of 66.9%). In conclusion, these two new formulae can be used as a screening tool for distinguishing cats with cardiac and non-cardiac diseases.

Keywords: cat, thoracic radiograph, cardiac disease, vertebral heart score

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Introduction

Feline heart disease can be divided into two categories, congenital and acquired heart diseases. Common acquired heart diseases in cats are hypertrophic cardiomyopathy (HCM), restrictive cardiomyopathy (RCM), dilated cardiomyopathy (DCM), and unclassified cardiomyopathy (UCM) (Payne et al., 2015). Several kinds of congenital defects have been reported in cats (Tidholm et al., 2015). The defect of the atrial and ventricular septum and atrioventricular valve dysplasia are popular in cats.

The diagnosis of feline heart disease basically begins with history taking and physical examination. Cats with heart disease may have unspecific clinical signs including vomiting, dyspnea, depress, poor appetite, restlessness, and paralysis due to arterial thromboembolism. Murmur, a good indicator for diagnosis of heart disease in dogs, may not be a helpful indicator in the case of cats. Previous studies reported apparent prevalence of heart murmurs in healthy cats between 15.5-33.7% (Paige et al., 2009; Wagner et al., 2010; Côté et al., 2004). On the other hand, murmurs can be found in only 50% of cats with cardiomyopathy (Côté et al., 2004; Ferasin et al., 2003). Thus, information from history and physical findings are not enough for screening or diagnosing heart disease in cats. Additional diagnostic methods are required to confirm suspicious patients before beginning any treatment.

Common cardiac diagnostic tests used currently include electrocardiography (ECG), thoracic radiography, cardiac biomarkers, and echocardiography. Electrocardiography is limited for identifying cardiac arrhythmias and conduction disturbances, but not the types of heart disease. The usefulness of cardiac biomarkers such as cardiac troponin I (cTnI) and N-terminal pro-brain natriuretic peptides (NT-proBNP) in feline medicine is currently uncertain. Echocardiography is the principal test for definitive diagnosis and identification of types of heart disease in cats. However, to perform echocardiography substantial skill in both acquisition and interpretation of data is required. Therefore, echocardiography is usually limited to referral centers or veterinary teaching hospitals. For these reasons, it is interesting to use thoracic radiography, which is less expensive, easier to access, and more practical as a screening tool for diagnosis of heart disease in cats.

The vertebral heart score (VHS) is a method for evaluating the dimensions of cardiac silhouette, described by Buchanan and Bucheler in dogs (Buchanan and Bucheler, 1995). Normal VHS values (≤8.1 vertebrae) have been established for cats (Lister and Buchanan, 2000). VHS is useful for evaluating cardiac enlargement associated with eccentric hypertrophy due to volume overload, but not concentric hypertrophy, which is a major type of cardiac structural remodeling in cats. A previous study by Sleeper et al. (2013) showed that VHS could be used to distinguish dyspneic cats with cardiac disease and non-cardiac disease. However, there is a gray zone (VHS between 8.0 and 9.3 vertebrae) that could not separate the cause of dyspnea clearly. Recently, Guglielmini et al. (2014) created the new indices for measurement of feline cardiac size; however, the diagnostic accuracy of these indices in discriminating between normal cats and cats with cardiac disease is only moderate.

As mentioned above, the measurement methods for evaluating feline cardiac size on thoracic radiographs used currently have some limitations. Therefore, this study was performed with an aim to create new methods for measuring cardiac size from thoracic radiographs, which can be used for distinguishing cats with cardiac disease and non-cardiac disease.

Materials and Methods

Cats: Medical records of cats presented at the Cardiology Unit of the Small Animal Veterinary Teaching Hospital of Chulalongkorn University from 2010 to 2015 were retrospectively reviewed. All cats recruited in the study had to undergo radiographic examination on the right lateral view and echocardiographic examination on the same day of thoracic radiographic examination. Only cats with good-quality thoracic radiographs were included in the study. Radiographs with incorrect position, vertebral abnormalities, and abnormalities obscuring the cardiac silhouette, e.g. pleural effusion and mediastinal mass, were excluded from the study. Digital radiographs from 49 cats were retrieved from the Imaging Unit, Small Animal Teaching Hospital, Faculty of Veterinary Science, Chulalongkorn University, Thailand. Echocardiography was used as a gold standard to diagnose cardiac disease and categorize the cats into two groups: cardiac disease (n=31) and non-cardiac disease (n=18).

Radiographic measurement: Five parameters modified from those of Lister and Buchanan (2000) were measured from the lateral radiographs including
1) the cardiac length (L), the length from carina to apex of the heart;
2) the cardiac width (W), the widest part of the heart perpendicular to L;
3) the width of the caudal vena cava (CVC), measured within two intercostal spaces from the caudal border of the heart;
4) the height of the spinous process of the fourth thoracic vertebrae (sT4), measured from the top of spinous process to the top of the 4th thoracic body; and
5) the length of the fourth sternal thoracic bone (S4) (Figure 1).

VHS was evaluated in all radiographs, as described by Litster and Buchanan (2000). The measurement was performed twice for each parameter by four different persons. Ten formulae were created and calculated including L•W, L•W/sT4, L•W/S4, L•W/CVC, (L+W)/S4, (L+W)/CVC, (L+W)xCVC, (L-W)/sT4, W/sT4, and CVC/S4.

Statistical analysis: Statistical analysis was performed using SPSS (22). The Shapiro-Wilk test was used to test the normality of data. The weight and age of cats in the cardiac and non-cardiac disease groups were compared with the independent t-test. Associations between age, sex, breeds, and weight and the evidence of cardiac disease diagnosed with echocardiography were tested by the Fisher exact test. Relationships between values of each parameter and formula and the evidence of cardiac disease were analyzed with the generalized linear mixed model. The receiver operating characteristic curve (ROC) was constructed to derive cut-offs for differentiation of cardiac and non-cardiac diseases. Sensitivity and specificity were calculated. The area under the curve (AUC) was evaluated to determine accuracy of the formulae (Gardner and Greiner, 2006).

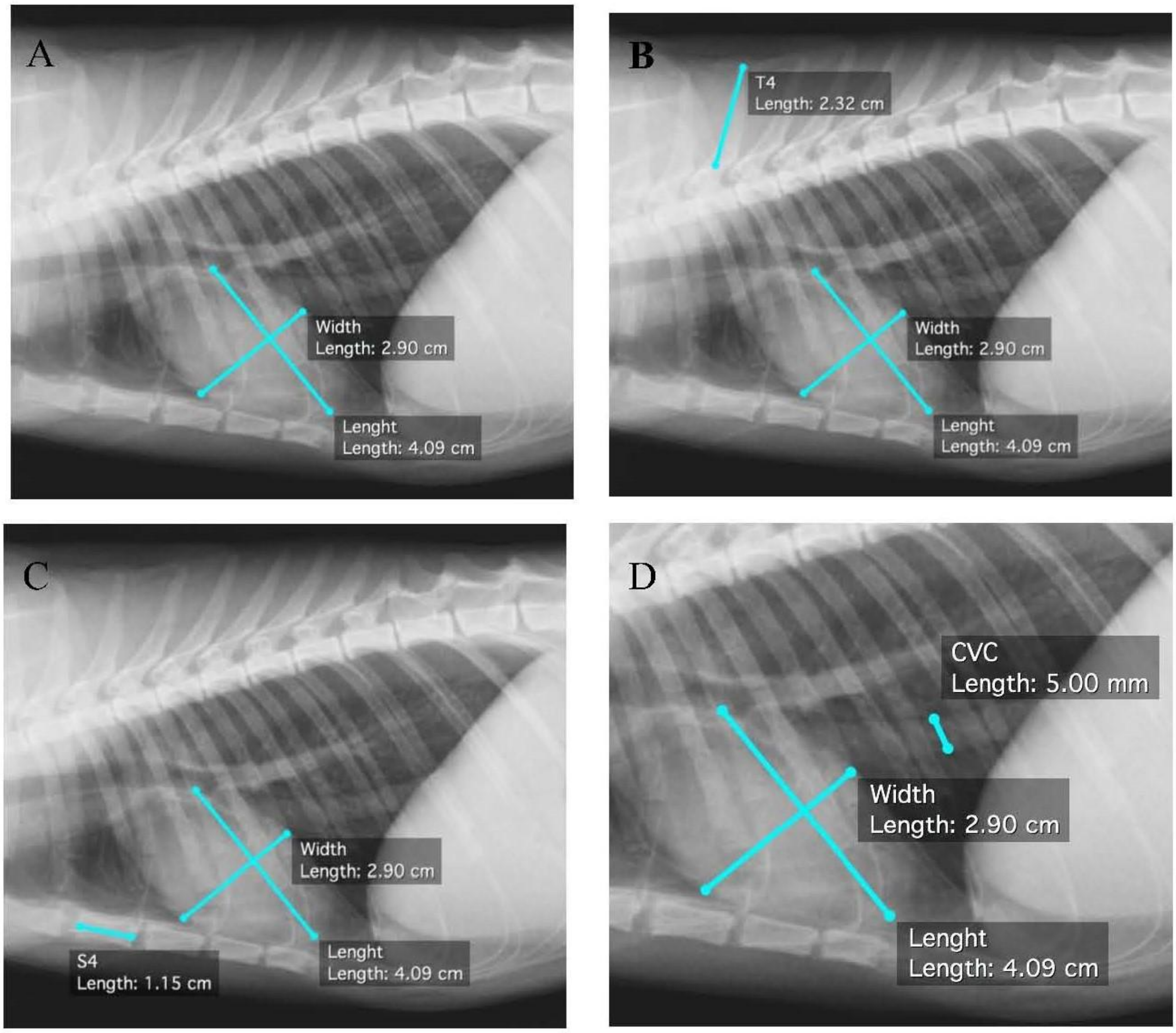

Figure 1 Illustrations demonstrating the measurement methods: (A) length (L) and width (W), (B) the height of the spinous process of the 4th thoracic vertebrae (sT4), (C) the length of the 4th sternal bone (S4), (D) the width of caudal vena cava (CVC)

Results

Radiographs from 49 cats were retrieved. All cats were older than one year, ranging from 2.9 to 12.5 years. Nineteen were male and thirty were female. Breeds of the cats included domestic shorthair (35), Persian (10), Wichian Mas (2), Kao Manee (1), and Korach (1). The characteristics of cats in the cardiac and non-cardiac groups are presented in Table 1.

Table 1 Characteristics of cats in the cardiac and non-cardiac groups

Cardiac group	Non-cardiac group
n=31	n=18
14 females and 17 males	16 females and 2 males
HCM (20), UCM (5), Pulmonic stenosis (1), hyperthyroidism induced cardiomyopathy (1), Tricuspid dysplasia (1), mitral valve stenosis (1), Double chamber left ventricle (1)	

HCM=hypertrophic cardiomyopathy; UCM=unclassified cardiomyopathy

Eighteen cats (16 females and 2 males) were in the non-cardiac disease group. Thirty-one cats (14 females and 17 males) were in the cardiac disease group. The cats in the cardiac disease group were diagnosed with HCM (20), UCM (5), mitral valve stenosis (1), pulmonic stenosis (1), hyperthyroidism induced cardiomyopathy (1), tricuspid dysplasia (1), mitral valve dysplasia (1), and double chamber left ventricle (1).

The mean weight of cats in the cardiac disease group (3.26±0.76 Kg) was not different from that in the non-cardiac disease group (3.85±1.13 Kg) (p=0.066). Also, the mean age of the cardiac disease group (8.03±5.03 years) was not different from that of the non-cardiac disease group (7.55±4.72 years) (p=0.744).

From the Fisher exact test, only sex (p=0.003), not age (p=0.483), weight (p=0.590) and breeds (p=0.367), had an association with the evidence of cardiac disease (T. The general linear mixed model analysis revealed the relationship between L, W, CVC, L•W, L•W/sT4, L•W/S4, SUM_{LW}/S4, and SUM_{LW}•CVC and the evidence of cardiac disease (Table 2)).

The results of receiver operating characteristic analysis are presented in Table 3.

Table 2 The general linear mixed model analysis of the relationship between L•W, L•W/sT4, L•W/S4, SUM_{LW}/S4, and M_{LW}•CVC and the evidence of the cardiac disease

Formula	Quartile	p-value	Odd ratio	95% Confident interval	
				Lower	Upper
L•W	Intercept	0.373	0.41	0.057	2.927
	Q1 <15.46			0	
	Q2 15.46-18.21	0.176	4.137	0.527	32.474
	Q3 18.21-22.49	0.044*	13.693	1.071	175.051
	Q4 22.49	0.006*	195.699	4.572	8375.991
L•W/T4	Intercept	0.574	0.589	0.092	3.754
	Q1 <5.91			0	
	Q2 5.91-6.77	0.152	4.127	0.592	28.742
	Q3 6.77-8.18	0.065	8.539	0.874	83.451
	Q4 >8.18	0.010*	50.559	2.557	999.815
L•W/S4	Intercept	0.382	0.424	0.062	0.908
	Q1 <11.89			0	
	Q2 11.89-14.32	0.210	3.772	0.471	Q2
	Q3 14.32-17.26	0.018*	21.341	1.702	Q3
	Q4 >17.26	0.004*	79.68	3.972	Q4
L•W/CVC	Intercept	0.349	2.321	0.397	13.566
	Q1 <26.36			0	
	Q2 26.36-29.31	0.981	0.978	0.156	6.139
	Q3 29.31-33.30	0.728	1.416	0.197	10.159
	Q4 >33.30	0.449	2.398	0.247	23.246
SUM_{LW}/S4	Intercept	0.905	0.892	0.136	5.862
	Q1 <6.07			0	
	Q2 6.07-6.75	0.346	2.558	0.362	18.091
	Q3 6.75-7.63	0.149	5.067	0.556	46.142
	Q4 >7.63	0.037*	19.04	1.19	304.619
SUM_{LW}/CVC	Intercept	0.078	5.368	0.83	34.712
	Q1 <12.39			0	
	Q2 12.39-14.00	0.667	0.638	0.082	4.966
	Q3 14.00-15.88	0.410	0.418	0.052	3.351
	Q4 >15.88	0.444	0.423	0.046	3.845
SUM_{LW}•CVC	Intercept	0.532	0.633	0.097	4.135
	Q1 <4.17			0	
	Q2 4.17-5.26	0.569	1.723	0.263	11.279
	Q3 5.26-7.09	0.144	5.815	0.545	61.993
	Q4 >7.09	0.012*	113.465	2.878	4473.933

*indicate statistical significance (p<0.05)

CVC=the width of caudal vena cava; L=length of the heart; S4=the length of the 4th sternal bone; sT4=the height of the spinous process of the 4th thoracic vertebrae; SUM_{LW}=summation of length and width of the heart; W=width of the heart; VHS=vertebral heart score

Discussion

The results of this study showed that sex, but not age, breed and weight, was related to the evidence of cardiac disease in cats. Male cats were more prone to develop cardiac disease than female cats. This result is in agreement with a previous study (Payne et al., 2015). The acquired cardiac disease was more prevalent than the congenital cardiac disease in the population of cats in this study. This result is consistent with a previous report (Guglielmini et al., 2014). Hypertrophic cardiomyopathy was the most frequently found cardiac disease, similar to a previous publication (Buchanan, 1999).

Five from the ten formulae created in this study were related to the occurrence of cardiac disease in this population of cats. These five formulae were L•W, L•W/sT4, L•W/S4, SUM_{LW}/S4, and SUM_{LW}•CVC.

Because the shape of the feline heart on the lateral thoracic view is similar to a rectangle, the formula L•W was created and applied from the mathematic equation for calculating an area of a rectangle. It was hypothesized that the area of the heart increased when the cat had heart disease. This hypothesis supports the finding of a recent study demonstrating an association between feline cardiac disease and an increased dimension of the overall cardiac silhouette, and of its long and short axes

(Guglielmini et al., 2014). The cut-off value of L•W to distinguish the cardiac and non-cardiac diseased cats was >16.45 cm^2 with 82.2% sensitivity and 66.9% specificity. With this cut-off value, the method provided the negative and positive predictive values of 72% and 81%, respectively.

The formulae L•W/sT4 and L•W/S4 were created to reduce variation of the area of the heart secondary to the size of the cats by dividing the area by the height of the spinous process of the 4th thoracic vertebrae or the length of the 4th sternal bone. These bones were selected because they can be viewed easily in every thoracic radiograph. Also, less dimension distortion is found on T4 and S4 because both bones are always in the center of the x-ray beam. The cut-off values of L•W/sT4 and L•W/S4 recommended in this study were >8.06 cm (sensitivity of 81.7% and specificity of 61.7%) and >12.85 cm (sensitivity of 81.7% and specificity of 66.9%), respectively. With the cut-off value of >8.06 cm, L•W/sT4 provided good sensitivity with 100% negative predictive value, but the positive predictive value was poor. With a very high negative predictive value, this method might be suitable to be used as a screening method to rule out cardiac disease in cats. L•W/S4 provided moderate negative and positive predictive values, with the recommended cut-off value of >12.85 cm.

Table 3 Receiver operating characteristic analysis

Formulae	AUC±SE	95% CI	Cut-off value	Sensitivity	Specificity	NPV	PPV	Inter-observer variability	Intra-observer variability
L•W	0.83±0.02	0.78-0.87	>12.06	1.00	0.11	5	100	8.47	3.27
			>16.45*	0.82	0.67	72	81		
			>23.64	0.30	1.00	100	35		
L•W/sT4	0.80±0.02	0.75-0.85	>7.50	1.00	0.01	89	52	7.25	3.83
			>8.06*	0.82	0.62	100	39		
			>9.31	0.20	1.00	100	19		
L•W/S4	0.82±0.02	0.77-0.86	>8.95	1.00	0.05	11	100	5.75	5.07
			>12.85*	0.82	0.67	61	90		
			>19.40	0.23	1.00	100	19		
SUM_{LW}/S4	0.76±0.03	0.71-0.81	>5.04	1.00	0.02	6	100	3.35	2.62
			>6.30*	0.81	0.56	56	87		
			>8.70	0.06	1.00	100	3		
SUM_{LW}•CVC	0.79±0.02	0.31-0.43	>2.41	1.00	0.01	0	100	14.55	2.64
			>4.52*	0.80	0.56	61	81		
			>9.37	0.17	1.00	100	16		
VHS	0.69±0.02	0.63-0.75	>8.0	0.63	0.77	56	64	3.25	2.68

*indicates statistical significance ($p<0.05$).

AUC = area under the curve (mean±standard error (SE)); CI=confidence interval; CVC=the width of caudal vena cava; L=length of the heart; NPV=negative predictive value; PPV=positive predictive value; S4=the length of the 4th sternal bone; sT4=the height of the spinous process of the 4th thoracic vertebrae; SUM_{LW}=summation of length and width of the heart; W=width of the heart; VHS=vertebral heart score

The summation of L and W was applied from VHS. However, the 4th sternal bone was used instead of the 4th thoracic vertebrae because the sternal bone never kinks even when the cat does not stretch well. In contrast, the thoracic vertebrae can easily be crooked when the cat is not in a good position. The recommended cut-off value of SUM_{LW}/S4 was >6.3 (sensitivity of 82.2% and specificity of 56%).

The summation of L and W multiplied by the width of CVC was created due to the relationship of the width of CVC to the occurrence of heart disease. The recommended cut-off value of SUM_{LW}•CVC was >4.52 (sensitivity of 80.4% and specificity of 55.6%). This method had a quite high inter-observer CV (14.55%). An increase in CV may be secondary to the variation of CVC measurements between each observer because there is no obvious landmark for the measuring location.

A previous study by Sleeper et al. (2013) used VHS measured from the right lateral view as a method to distinguish dyspneic cats with cardiac and non-cardiac diseases. The cut-off value of 8.0 was recommended in that study. With that cut-off value, VHS provided sensitivity of 62.6% and specificity of 76.7% to differentiate between the cardiac and non-cardiac diseases in the population of cats in the present study. This finding suggests that VHS is a method that has higher specificity to identify heart disease in cats than the new formulae created in the present study. However, the formulae had higher sensitivity when compared to VHS, suggesting that the newly created formulae in this study might be a better screening tool for separating cats with cardiac and non-cardiac diseases.

The first limitation of this study is the low number of cats recruited. The second limitation is the wide age range of cats used in this study. Cats may have different cardiac shape by thoracic radiography depending on the span of age (Moon et al., 1993; Guglielmini and Diana, 2015). This variation may affect the results of this study. Lastly, all of the measurement was performed on the right lateral view only. The evaluation of cardiac dimension on two radiographic views together may enhance the accuracy. In the present study, the cardiac size only on the right lateral view was evaluated because sometimes it is difficult to perform more than one position of thoracic radiography in cats with heart disease, particularly in the case of congestive heart failure. To adjust the position of cats to the right lateral recumbency is easier and less stressful than other positions. Also, the right lateral view has been recommended to be used as the primary view for evaluation of cardiovascular abnormalities in cats because it provides more information about cardiac shape, left atrial size, vascular patterns, and lung parenchyma abnormalities (Guglielmini and Diana, 2015).

This study recommends the formulae L•W and L•W/S4 because they provide good sensitivity with moderate negative and positive predictive values, suitable to be a screening method for diagnosing cardiac disease in cats. However, the specificity of these formulae is moderate. Thus, these formulae should be used for screening but not for definitive diagnosis of heart disease in cats. The radiographic examination and the formulae created in this study may not be useful in case of the silhouette sign, in which the border of the heart cannot be differentiated well. Another limitation of radiography in terms of the diagnosis of cardiac disease in cats is that the shape and area of the heart may depend on the type and severity of the cardiac disease, i.e. a heterogenous pattern of cardiac remodeling. For example, cats with hypertrophic cardiomyopathy may have concentric hypertrophy secondary to an abnormal growth of cardiac muscles, but cats with atrioventricular valve dysplasia may have eccentric hypertrophy due to volume overload. In some cases such as cardiomyopathies that are usually associated with no or mild left ventricular chamber enlargement, radiography may underestimate and be less accurate in recognizing the cardiac disease in cats. Thus, echocardiography should be performed in all suspicious cats to confirm and diagnose the heart disease.

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บทคัดย่อ

วิธีการใหม่ในการแยกแยะแมวที่เป็นและไม่เป็นโรคหัวใจจากภาพถ่ายรังสีทรวงอก

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วัตถุประสงค์ของการศึกษานี้เพื่อจำแนกระหว่างแมวที่เป็นและไม่เป็นโรคหัวใจด้วยพารามิเตอร์ต่างๆ ที่ได้จากภาพถ่ายรังสีทรวงอก การศึกษานี้ทำในประชากรแมวจำนวน 49 ตัว อายุเฉลี่ย 7.72±4.79 ปี คละน้ำหนัก เพศ และพันธุ์ ใช้คลื่นเสียงสะท้อนหัวใจความถี่สูงเป็นวิธีมาตรฐานในการวินิจฉัยยืนโรคหัวใจและแยกแมวออกเป็น 2 กลุ่ม คือ แมวที่เป็นโรคหัวใจ 31 ตัว และไม่เป็นโรคหัวใจ 18 ตัว ทำการวัด 5 พารามิเตอร์จากภาพถ่ายรังสีในท่านอนตะแคงขวา ได้แก่ 1) ความยาวของหัวใจ (L); 2) ความกว้างของหัวใจ (W); 3) ความกว้างของหลอดเลือดเวนาคาวาส่วนท้าย (caudal vena cava หรือ CVC); 4) ความสูงของสไปนัส โปรเซส (spinous process) ของกระดูกสันหลังส่วนอกท่อนที่ 4 (sT4); และ 5) ความยาวของกระดูกสันอก (sternum) ท่อนที่ 4 (S4) นำ 5 พารามิเตอร์ดังกล่าวไปสร้างเป็นสมการทั้งหมด 10 สมการ พบว่ามี 5 สมการที่ข้อมูลระหว่างแมวกลุ่มที่เป็นและไม่เป็นโรคหัวใจมีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ($p<0.05$) ได้แก่ L•W, L•W/sT4, L•W/S4, SUM_{LW}/S4 และ SUM_{LW}•CVC สมการที่ผู้ทำการศึกษาแนะนำ คือ L•W (ค่าจุดตัด >16.45 ตารางเซนติเมตร; ความไว 82.2% และความจำเพาะ 67%) และ L•W/S4 (ค่าจุดตัด >12.85 เซนติเมตร; ความไว 81.7% และความจำเพาะ 66.9%) โดยสรุปการประเมินภาพถ่ายรังสีทรวงอกด้วยสมการใหม่ 2 สมการนี้สามารถใช้เป็นวิธีการคัดกรองเบื้องต้นเพื่อแยกแมวที่เป็นและไม่เป็นโรคหัวใจ

คำสำคัญ: แมว ภาพถ่ายรังสีทรวงอก โรคหัวใจ วิธีการวัดขนาดของหัวใจเทียบมาตราส่วนกับกระดูกสันหลัง

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